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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/980,751	11/01/2001	Alan T. Remaley	15280-3931US	7562

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EXAMINER	
VENCI, DAVID J	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 01/26/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/980,751	REMALEY ET AL.	
	Examiner	Art Unit	
	David J. Venci	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *October 18, 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *7* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 8-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-21* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *November 1, 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 18, 2005, is entered. Currently, claims 1-6 and 8-21 are under examination.

Drawings

Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

The drawings are objected to because the drawings do not indicate figure numbers for each figure.

Claim Rejections - 35 USC § 112 – first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6, 18 and 20-21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Dependent claims 6, 18 and 20-21 recite an "antibody" species elected for examination in Applicants' reply, dated November 8, 2004. Claims 6, 18 and 20-21 encompass, *inter alia*, a method of determining cholesterol comprising two steps: (1) forming a complex between said "antibody" and a "fraction", followed by (2) dissociating said "antibody" from said "fraction".

Applicants' specification discloses forming a complex between an antibody and apolipoprotein B (see *e.g.*, Examples 1 and 2, specifically p. 25, lines 7-10) using a "EZ-HDL™" kit from Sigma Diagnostics, Inc. Applicants' specification appears to disclose that forming said complex results in immunoprecipitation (see p. 22, line 18-19, "[t]he HDL precipitation method was performed..."). After forming said complex, Applicants' specification teaches an additional step of adding deoxycholate to said complex (see *e.g.*, Table 1, Step 3).

With respect to step (1), *supra*, Applicants' specification does not appear to disclose a specific antibody, or whether immunoprecipitation is necessary, or the extent of immunoprecipitation necessary for completing the step of forming a complex between an antibody and apolipoprotein B.

With respect to step (2), *supra*, Applicants' specification does not appear to explicitly disclose an additional step of dissociating said "antibody" from said "fraction". Applicants' specification does not appear to set forth any causal relationship between the step of adding deoxycholate with the step of dissociating said "antibody" from said "fraction". Applicants' specification does not appear to disclose the necessary experimental parameters necessary for completing the step of dissociating said "antibody" from said "fraction". Applicants' specification does not appear to disclose a specific antibody and a corresponding deoxycholate concentration necessary for completing the step of dissociating said "antibody" from said "fraction". Applicants' specification does not appear to disclose the contents, ingredients, or method steps of a "EZ-HDL™" kit from Sigma Diagnostics, Inc. necessary for completing the step of dissociating said "antibody" from said "fraction".

According to the decision in *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), the factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include:

(A) The breadth of the claims;

(B) The nature of the invention;

(C) The state of the prior art;

(D) The level of one of ordinary skill;

(E) The level of predictability in the art;

(F) The amount of direction provided by the inventor;

(G) The existence of working examples; and

(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Here, the nature of Applicants' invention appears to involve a procedural modification to a commercial kit sold as "EZ-HDL™" kit from Sigma Diagnostics, Inc. Examiner posits that the contents, ingredients, and method steps of a "EZ-HDL™" kit from Sigma Diagnostics, Inc. is not common knowledge among persons of ordinary skill. Examiner posits that persons of ordinary skill do not have the requisite level of skill necessary to determine the contents or ingredients of a "EZ-HDL™" kit from Sigma Diagnostics, Inc. Examiner posits that persons of ordinary skill recognize that the contents, ingredients and method steps of commercial kits are often optimized for exact and controlled experimental conditions, deviations from which result in non-optimal results. Examiner posits that the amount of direction provided by Applicants, by way of Examples 1 and 2, is not sufficient to enable persons of ordinary skill to discern the contents or ingredients of a "EZ-HDL™" kit from Sigma Diagnostics, Inc.

In conclusion, the quality and quantity of Applicants' disclosure is insufficient such that Applicants' invention requires undue experimentation to make and use Applicants' invention.

Claim Rejections - 35 USC § 112 – second paragraph

Claims 1-6 and 8-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1, step (a), the recitation of the pronoun "which" is indefinite. The identity of any object(s) defining the class "which" is/are not clear.

In claim 1, step (a), the recitation of "forms a complex" is indefinite. Whether said "complex" exists in a solid phase (e.g. a precipitated complex) and/or liquid phase (e.g. dissolved in solution) is not clear. Whether said solid phase complex, if any, is present during measurement is not clear. Whether said solid phase complex, if any, is removed prior to measurement is not clear.

In claim 1, step (c), the recitation of "dissociating the first lipoprotein fraction from the complex-forming agent" is indefinite. Whether said "dissociating" occurs in a solid phase (e.g. a precipitated complex) and/or liquid phase (e.g. dissolved in solution) is not clear. Whether said "dissociating" requires step(s) of precipitation, centrifugation and/or dissolution is not clear.

In claims 1, 4-6, 17 and 19, the recitation of "fraction" is indefinite. Whether/how a sample is fractioned or fractionated, or what mathematical operation(s) is/are required for the determination of "fraction" or what physical parameter(s) consist or comprise "fraction" is/are not clear. In claim 1, the recitation of "fraction present in the sample" is indefinite because whether/how said fractions are created, identified, isolated, separable, distinguishable, or are physically divided from the rest of the sample is not clear. In claim 1, the recitation of "a second lipoprotein fraction" is indefinite. Whether/how said second fraction is created, identified, isolated, separable, distinguishable, or is physically divided from the first lipoprotein fraction or from the rest of the sample is not clear.

In claims 10-11, the recitation of "the measuring of the amount of cholesterol present in steps (b) and (d) is performed by reacting... with cholesterol esterase" renders claim 1 indefinite. It is not clear how it is possible to measure the total amount of cholesterol in step (d) when an amount of cholesterol was already consumed by reaction with cholesterol esterase in step (b). Similarly, in claim 11, the recitation of "said cholesterol is reacted with cholesterol oxidase or cholesterol dehydrogenase" renders claim 1 indefinite because it is not clear how it is possible to measure the total amount of cholesterol in step (d) when an amount of cholesterol was already consumed by reaction with cholesterol oxidase or cholesterol dehydrogenase in step (b).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-6, 8-17 and 19-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Kerscher *et al.* (US 4,851,335).

Kerscher *et al.* describe a method for determining amounts of cholesterol (see Title, "determination of HDL cholesterol") in a first lipoprotein fraction (see col. 2, lines 22-29, "HDL-cholesterol", "LDL-cholesterol, VLDL-cholesterol") and a second lipoprotein fraction (see col. 2, lines 22-29, "HDL-cholesterol", "LDL-cholesterol, VLDL-cholesterol") in a sample (see col. 2, lines 22-29, "serum or plasma") comprising the steps of: adding a complex-forming agent (see col. 2, lines 39-40, "salt of a bile acid or a bile acid derivative or of dioctylsulphosuccinate"), measuring the amount of cholesterol associated with the second lipoprotein fraction (see col. 2, lines 40-41, "a first measurement is then carried out"), dissociating the first lipoprotein fraction from the complex forming agent (see col. 2, lines 53-57, "in a second incubation step, by the addition of a non-ionic, polyethylene oxide group-containing detergent, or of a secondary alkane sulphonate"), measuring the total amount of cholesterol (see col. 2, line 61, "total cholesterol"), subtracting the amount of cholesterol associated with the second lipoprotein fraction from the total amount of cholesterol (see col. 2, lines 45-46, "the difference between the first and second measurement").

Kerscher *et al.* describe a complex-forming agent (see col. 2, lines 39-40, "salt of a bile acid or a bile acid derivative or of dioctylsulphosuccinate") that necessarily forms a complex with the first lipoprotein fraction,

and would be so recognized by persons of ordinary skill. See *e.g.*, Salvioli *et al.*, 187 FEBS LETT. 272 (1985).

With respect to claims 6 and 20, Kerscher *et al.* describe immunoprecipitation of lipoproteins (see col. 2, lines 5-6, "immune precipitation").

With respect to claims 8-9, Kerscher *et al.* describe deoxycholate (see col. 3, line 43, "deoxycholic acid").

Claims 1-6, 8-17 and 19-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Pascal (US 4,366,244).

Pascal describes a method for determining amounts of cholesterol (see Title, "measuring serum cholesterol") in a first lipoprotein fraction (see Abstract, "various fractions") and a second lipoprotein fraction (see Abstract, "various fractions") in a sample (see Title, "serum") comprising the steps of: adding a complex-forming agent (see col. 4, lines 41-42, "precipitation with systems such as polyanions (heparin..."), measuring the amount of cholesterol associated with the second lipoprotein fraction (see col. 7, lines 19-20, "measure only one of the isolated fractions"), dissociating the first lipoprotein fraction from the complex forming agent (see col. 6, line 50, "[t]he precipitate must be dissolved"), measuring the total amount of cholesterol (see col. 7, lines 21-22, "a conventional method of determining the total cholesterol"), subtracting the amount of cholesterol associated with the second lipoprotein fraction from the total amount of cholesterol (see col. 7, lines 22-23, "taking the difference, at the missing value").

Response to Arguments

In prior Office Action, claims 17 and 19 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for the recitation of "fraction consists of... in the sample". Specifically, how a fraction *consisting of* a particular lipoprotein can be created, identified, isolated, separable, distinguishable, or is physically divided from a sample (e.g. serum, plasma) when the sample comprises lipoproteins and many other components was considered unclear. This rejection is withdrawn.

In prior Office Action, claims 10-11 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for the recitation of "the measuring of the amount of cholesterol present in steps (b) and (d) is performed by reacting... with cholesterol esterase". Specifically, the possibility of measuring the total amount of cholesterol in step (d) when an amount of cholesterol was already consumed by reaction with cholesterol esterase/oxidase/dehydrogenase in step (b) was not clear. In response, Applicants appear to restate the steps recited in step (d) of claim 1. Applicants' restatement is noted.

In prior Office Action, claims 1-6 and 8-21 were rejected under 35 U.S.C. 102(e) as being anticipated by Miki et al. (US 6,162,607). Applicants' amendment to the claims and/or argumentation are fully persuasive and sufficient to overcome this rejection. Accordingly, this rejection is withdrawn.

Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Venci whose telephone number is 571-272-2879. The examiner can normally be reached on 08:00 - 16:30 (EST). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

David J Venci
Examiner
Art Unit 1641

djv

LONG V. LE
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01/20/06